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Characteristics of Special Circulations

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Keywords; autoregulation; myogenic theory; metabolic theory; cerebral; coronary; renal; hepatic; pulmonary blood flow; adenosine; vasoactive metabolites;

Abstract

Blood flow through a vascular bed is usually determined by the pressure gradient across it and the diameter of the precapillary resistance vessels. Special circulations have additional specific features of blood flow control. Several organs control their blood supply by autoregulation. Coronary blood flow is linked to myocardial oxygen consumption, primarily by a metabolic mechanism, thus increases in demand, or decreases in supply, of oxygen cause the release of vasodilator metabolites, which act on vascular smooth muscle to cause relaxation and hence increase blood flow. Cerebral blood flow is primarily regulated by a myogenic mechanism whereby increases in transmural pressure stretch the smooth muscle, which responds by contracting, however, this can be overridden by cerebral tissue PCO₂. Further, the cerebral circulation is contained in a rigid structure (the skull) that has additional consequences for blood flow after brain injury, when the pressure within this compartment may rise dramatically. Renal blood flow is regulated by both extrinsic and intrinsic mechanisms; sympathetic vasoconstriction of the afferent arterioles reduces renal blood flow in response to a decrease in effective circulating volume, myogenic mechanisms and tubuloglomerular feedback, as well as the release of vasoactive metabolites from the vascular endothelium regulate renal blood flow intrinsically. Hepatic blood flow is delivered via the hepatic artery and the portal vein, and the amount varies reciprocally to maintain total blood flow constant. The pulmonary circulation receives the entire cardiac output and blood flow is regulated both passively and actively. Pulmonary vessels are highly distensible and can accommodate increases in blood flow without significant increases in pressure. However, this leads to regional differences in blood flow throughout the lung. Regional reductions in alveolar oxygen tension constrict local arterioles to divert blood to better ventilated areas.

In 'special circulations' additional factors govern the control of blood flow, beyond the 'standard' mechanisms that prevail in most organ systems (see article Control of the Circulation). In this article the coronary, cerebral, renal, hepatic and pulmonary 'special' circulations are considered.

Blood flow through the cardiovascular system is dependant on the force driving blood along the vessel (pressure gradient) and is restricted by the resistance of the vessels. The resistance to blood flow, in turn is dependent on the radius and length of the blood vessel and the viscosity of the blood flowing through it. In practice it is the resistance of the arterioles that normally has the greatest effect on blood flow. An approximate relationship between vessel dimensions and blood viscosity is shown in Equation 1 (below).

Poiseuille's law is an approximation for the cardiovascular system since Poiseuille's law strictly should only be applied to Newtonian fluids flowing through a straight unbranched, non-distensible, tube; conditions that do not prevail in the cardiovascular system. However, the equation does give a useful approximation for the cardiovascular system.

$$Q = \frac{\pi(P_1 - P_2) r^4}{8\eta l}$$

Poiseuille's law; Q = blood flow, $P_1 - P_2$ = the pressure gradient (normally arterial minus venous), r = radius of the vessel, η = viscosity, l = length of the vessel, $\pi/8$ = constant of proportionality.

In Poiseuille's Law radius of the vessel is raised to the power 4, thus if the radius were to double, flow would increase 16-fold. The most important vessels regulating blood flow in this manner are the small arteries and arterioles as they contain an abundance of vascular smooth muscle arranged in a circular manner along the length of the vessel, the tone of which is regulated by both extrinsic (neural and humoral) and intrinsic (myogenic and metabolic) factors.

Extrinsic control

The major vasomotor nerves are vasoconstrictor sympathetic fibres, which have tonic activity, accounting for the basal tone in resistance vessels. The primary neurotransmitter released from sympathetic nerve terminals is noradrenaline (NA) acting on the α and β -adrenoreceptors. In many vascular beds the sympathetic system is associated with activation of α -adrenoreceptors to mediate a vasoconstriction. Only a small proportion of the resistance vessels in the body receive a parasympathetic (vasodilator) nerve supply, e.g., the cerebral and meningeal blood vessels, parts of the viscera, genitalia, large bowel and bladder, but not skeletal muscle or skin. The vasodilation of cutaneous blood vessels in association with sweating may be partly due to the production of a vasodilator polypeptide bradykinin within exocrine glands.

Adrenaline has varying effects on vessel diameter, and hence blood flow; in skeletal muscle low concentrations of adrenaline act on the β -adrenoreceptors to induce vasodilation, whereas in high concentrations acts on the α -adrenoreceptors to induce vasoconstriction. NA, however, is always a vasoconstrictor. Other vasoconstrictor hormones include angiotensin II and vasopressin.

Intrinsic control

Intrinsic control refers to local control within a vascular bed rather than a centrally-mediated reflex control. Local control of the circulation can be divided into direct effects on vascular smooth muscle and indirect effects via the vascular endothelium.

Properties of vascular smooth muscle

A number of vascular beds can maintain a constant blood flow despite variations in arterial blood pressure (within limits). This is termed autoregulation. In addition, many organs adjust blood flow to match metabolic activity. This type of local regulation occurs independently of both the endothelium and nervous input, and is the

result of direct changes in vascular tone. There are currently two main theories to explain autoregulation of blood flow:

Myogenic mechanism

Increased tension in the blood vessel wall stretches the vascular sarcolemma. The vascular muscle responds by contracting, and increasing resistance to maintain pressure, and hence blood flow, constant.

Metabolic mechanism

In certain organs blood flow is regulated to match metabolic activity of the tissue. A decrease in supply or an increase in demand of oxygen causes the tissue to release vasodilator metabolites such as;

- potassium ions
- hydrogen ions (lactic acid)
- phosphate ions
- carbon dioxide
- prostaglandins
- adenosine

These act locally, directly influencing vascular smooth muscle to cause relaxation and an increase in blood flow. This is called functional hyperaemia. A decrease in metabolic activity will decrease the formation of vasodilator metabolites, and hence lead to vasoconstriction. There is normally a background level of metabolites in the tissue so this mechanism can also form the basis of autoregulation. An increase in blood pressure can increase blood flow (Equation 1). This will cause a 'wash-out' of vasodilator metabolites leading to a loss of vasodilator influence and hence a vasoconstriction, reducing blood flow back to the original level.

Properties of the endothelium

The vascular endothelium can also influence local blood flow. Endothelial cells produce and release both vasodilator and vasoconstrictor metabolites in response to a variety of stimuli such as shear stress due to increased blood flow and hypoxia. Nitric oxide (NO) is perhaps the most important of the vasodilator substances (see *Anaesthesia & Intensive Care Medicine* 2:2: 77).

The relative importance of these different regulatory mechanisms of regional blood flow differs between different vascular beds and at different times within the same vascular bed.

Coronary circulation

The myocardium receives its entire nutritional blood supply from the coronary arteries. The right coronary artery mainly supplies the right atrium and ventricle, the left coronary artery divides into the anterior descending and circumflex branches and mainly supplies the left atrium and ventricle.

Control of myocardial blood flow

The primary factor responsible for perfusion of the myocardium is aortic pressure. However, moment-to-moment coronary blood flow (CBF) is strongly influenced by mechanical activity of the heart. The coronary blood vessels course through the myocardium and are thus compressed during systole. Thus, CBF is greatest during

early diastole when extravascular compression is minimal and aortic pressure is still high, and lowest during isovolumetric contraction when extravascular compression can interrupt, or even reverse blood flow in the left ventricular coronary vessels (Figure 1). Tachycardia (reduced diastolic time), elevations in end-diastolic pressure, and reduced arterial pressure will all result in a reduction in CBF. Compression of the coronary arteries is greatest near the endocardial surface and diminishes nearer the epicardial surface. Thus, it is vessels in the left ventricular inner wall which are most susceptible to ischaemic damage in coronary artery disease.

CBF is tightly linked to myocardial oxygen consumption, primarily by the metabolic mechanism. In contrast to most tissues, cardiac tissue extracts oxygen maximally even under normal conditions. The heart therefore adjusts its blood flow to meet its metabolic needs. Adenosine appears to play a significant role in metabolic vasodilation under pathophysiological conditions such as ischaemia, but may not be involved in matching CBF to myocardial metabolism under physiological conditions such as exercise (1). Numerous other agents may be involved in functional hyperaemia (hypoxaemia, hypercarbia, potassium and hydrogen ions) but the full mechanism is yet to be determined.

Cardiac nerve activity has little influence on CBF. Activation of cardiac sympathetic nerve fibres initially constricts, and vagal nerve activity initially slightly relaxes the coronary resistance vessels. However, the resulting changes in metabolic work have a far more potent effect on vascular tone.

Cerebral circulation

Blood flow to the brain is via the internal carotid and vertebral arteries, which anastomose to form the circle of Willis. The brain is particularly intolerant of periods of ischaemia. Indeed, interruption of cerebral blood flow for as little as 5 seconds results in loss of consciousness, and irreversible cell damage occurs within minutes. Cerebral blood flow will be maintained at the expense of other organs in situations of reduced cardiac output, such as haemorrhage.

The whole of the cerebral circulation lies within a rigid structure, the cranium, the contents of which are essentially incompressible (see *Anaesthesia & Intensive Care Medicine* 2:8: 293). Following head injury cerebral oedema occurs which may lead to intracranial hypertension. Under these conditions cerebral perfusion pressure is governed by the difference between arterial pressure and intracranial pressure (ICP) rather than the usual arterio-venous pressure difference. Increased ICP following head injury will reduce cerebral blood flow and may lead to cerebral ischaemia. Recent studies suggest that resuscitation with hypertonic solutions may reduce ICP in these circumstances.

Control of cerebral blood flow

Total cerebral blood flow is maintained within tight limits to ensure an uninterrupted supply of oxygen to the brain, although local neuronal activity is associated with changes in regional cerebral blood flow via metabolic substances. Extrinsic control of total cerebral blood flow appears to be weak and mainly affects larger cerebral vessels, whereas the cerebral resistance vessels are regulated under a well-developed intrinsic mechanism. Autoregulation of total cerebral blood flow is apparent within the range

of 60-180 mmHg arterial pressure, and this is likely to be due to a myogenic mechanism, but this range may be right-shifted by sympathetic nerve activity or chronic systemic hypertension. Cerebral myogenic autoregulation can be overridden by changes in arterial carbon dioxide tension; even small degrees of hypercapnia cause vasodilation and hypocapnia leads to vasoconstriction. Hypoxaemia also causes cerebral vasodilation at thresholds which may be as high as 8.5kPa. The vasodilatory effects of hypercapnia but not hypoxaemia, appear to be mediated by NO from the endothelium (see *Anaesthesia & Intensive Care Medicine* **2:2**: 77).

Renal circulation

Blood flow to the kidneys is via the renal arteries, which eventually branch to form the afferent arterioles, glomerular capillaries and efferent arterioles. This arrangement aids tight regulation of renal blood flow (RBF) and, indirectly, glomerular filtration (GFR).

Control of renal blood flow

RBF is regulated by both extrinsic and intrinsic mechanisms. Autoregulation of RBF occurs over the range of pressures 90-180 mmHg by two mechanisms; the myogenic mechanism and tubuloglomerular feedback, whereby changes in tubular flow rate are detected by the cells of the macula densa, which in turn leads to changes in afferent arteriolar diameter, to alter glomerular capillary hydrostatic pressure and hence control GFR. It has been suggested that the variable sensed is NaCl concentration of tubular fluid and the likely effector mediators are adenosine, (which, in this instance constricts the afferent arteriole) and NO. Stimulation of renal sympathetic nerves cause an α -adrenoreceptor-mediated vasoconstriction of both afferent and efferent arterioles, but primarily affects afferent arterioles; e.g., sympathetic vasoconstriction of the afferent arterioles occurs in response to strong emotional stimuli and decreases in effective circulating volume to decrease RBF. Endothelial cells also play an important role in regulating in RBF (Figure 2).

Hepatic circulation

The liver receives three quarters of its blood supply from the portal vein (PV; formed from the superior mesenteric and splenic vein) and the rest from the hepatic artery (HA; a branch of the coeliac trunk). As the PV has already passed through the spleen and gastrointestinal circulation oxygen saturation is low. However, blood in the HA is fully saturated. The PV and HA branch to form the terminal portal venules and hepatic arterioles, both of which contain vascular smooth muscle, and drain into the sinusoids (capillary network) in the acinus.

Control of hepatic blood flow

Blood flow in the PV and HA varies reciprocally in an attempt to maintain hepatic blood flow. However, the increase in blood flow in one vessel doesn't fully compensate for reductions in the other. The hepatic arterial buffer response (HABR) normally maintains blood flow and hence oxygen delivery constant to the liver at times of reduced portal venous flow and is thought to be mediated by adenosine. Thus under normal conditions adenosine is constantly washed out by portal venous blood flow, however, under conditions of decreased portal venous flow adenosine

accumulates and, due to the close proximity of the PV and HA, leads to dilation of the hepatic arterioles and increases in blood flow.

The PV and HA are innervated by noradrenergic sympathetic nerves, activity in which reduces blood flow during low flow states such as hypovolaemia. However, stimulation of hepatic nerves has a more significant effect on capacitance vessels and can mobilise about half of the hepatic blood volume following haemorrhage.

Pulmonary circulation

The pulmonary circulation is a low resistance (one tenth of systemic), low pressure, high flow network with a very high density of capillaries. Pulmonary arterioles have very little vascular smooth muscle and so do not have the same capacity for vasoconstriction as do systemic arterioles. However, this structure matches its function in that it is required to accept the entire cardiac output at all times, whilst minimising right ventricular work.

Passive regulation of pulmonary blood flow

Large increases in flow (as in exercise) can be accommodated with only small increases in pressure, thus resistance must fall further. This is achieved by recruitment and distension of capillaries. Lung volume also has effects on pulmonary vascular resistance (PVR); at low and high lung volumes resistance is high, and lowest at functional residual capacity. The low pressures and high distensibility of the pulmonary vessels mean that gravity causes regional variations in blood flow within the lung, which is affected by posture and exercise. In the upright individual flow is greatest at the bottom of the lung due to the hydrostatic pressure of the 'column' of blood above it. Flow at the apices is thus lowest and in conditions of low pulmonary arterial pressure such as hypovolaemia, or positive pressure ventilation, intravascular pressure may fall below extravascular (alveolar) pressure in this region leading to cessation of blood flow and reduced gas exchange.

Active regulation of pulmonary blood flow

Pulmonary arterioles are innervated by the autonomic nervous system and PVR may be altered by stimulation of the baro and chemoreceptor reflexes. However, the main influence on PVR is hypoxia. Regional reductions in alveolar oxygen tension constrict local arterioles (opposite to systemic effects) to divert blood to better ventilated areas and thus optimise the ventilation:perfusion ratio (Figure 3). However if more than 20% of the lung is involved this may increase overall PVR and lead to pulmonary hypertension and pulmonary oedema.

Figure 1

NOTE: FOR THIS FIGURE PLEASE USE A FIGURE PREVIOUSLY PUBLISHED IN ANAESTHESIA AND INTENSIVE CARE MEDICINE 2:1 (feb), pg14 fig 1

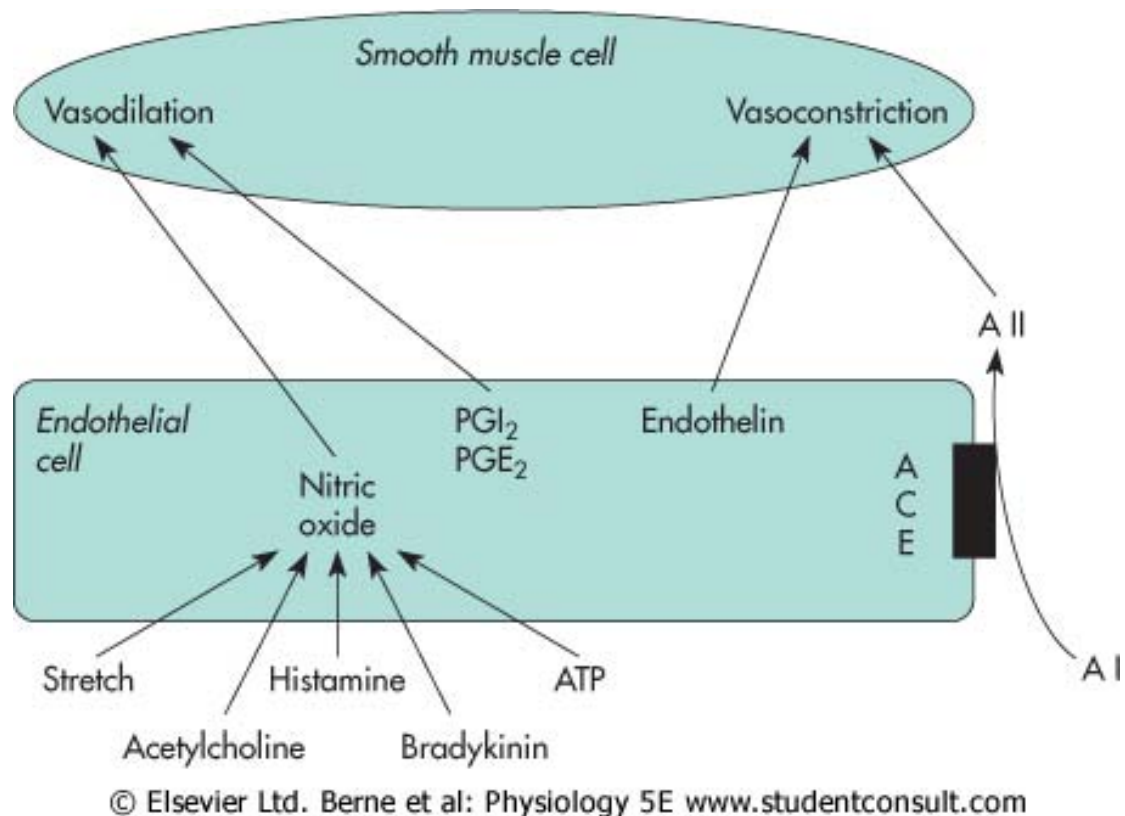


Figure 2 Role of endothelial cells in renal afferent and efferent arteriolar vascular tone

Endothelial cells produce several vasoactive hormones which act on the smooth muscle cells to regulate RBF. *ACE*, angiotensin converting enzyme; *AI*, angiotensin I; *AII*, angiotensin II; *PGI₁*, prostaglandin I₁; *PGE₂*, prostaglandin E₂.

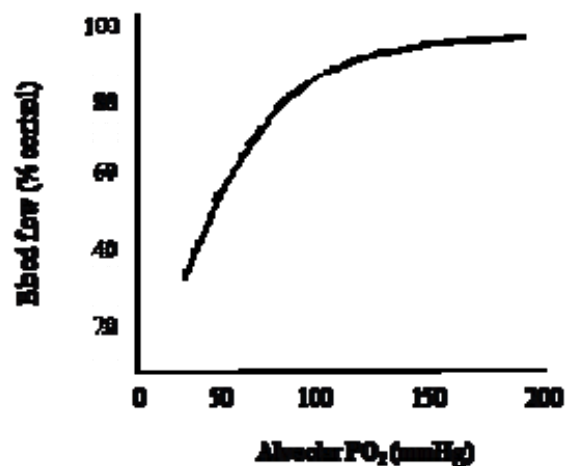


Figure 3 Regional reductions in alveolar oxygen tension reduce local blood flow

Hypoxia induces local increases in pulmonary vascular resistance and hence a fall in regional blood flow to divert blood to better-ventilated areas.

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